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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 02/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,571	LASKEN ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,11-15,20-25,27,29,31-33,35-39,41,42,44-49,51-53 and 55-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,11-15,20-25,27,29,31-33,35-39,41,42,44-49,51-53 and 55-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to an amendment filed November 24, 2004. Claims 1, 5-9, 11-15, 20-25, 27, 29, 31-33, 35-39, 41, 42, 44-49, 51-59 and 61 were previously pending. Applicants amended claim 35 and cancelled claims 54 and 61. Claims 1, 5-9, 11-15, 20-25, 27, 29, 31-33, 35-39, 41, 42, 44-49, 51-53 and 55-59 are pending and will be examined.

2. Applicants' amendments and arguments overcame the following: objection to claims 54 and 61; rejection of claim 35 61 under 35 U.S.C. 112, second paragraph; rejection of claims 1, 5-9, 11-15, 20-25, 27, 29, 31-33, 35-39, 41, 42, 44-49, 51-59 and 61 under 35 U.S.C. 112, first paragraph, written description; rejection of claims 1, 5-8, 11, 13, 15, 20, 21, 24, 27, 29, 31-33, 35, 38, 39, 41, 42, 44-49, 51-54 and 61 under 35 U.S.C. 103(a) over Dean et al. and Eckstein et al.; rejection of claims 12, 22, 23, 36 and 37 under 35 U.S.C. 103(a) over Dean et al. and Eckstein et al. in view of Rothberg et al.; rejection of claims 14, 25, 57 and 58 under 35 U.S.C. 103(a) over Dean et al. and Eckstein et al. in view of Navarro et al.; rejection of claims 55 and 56 under 35 U.S.C. 103(a) over Dean et al. and Eckstein et al. in view of Sorge et al. All other rejections are maintained for reasons given in the "Response to Arguments" section below.

Response to Arguments

3. Applicant's arguments filed November 24, 2004 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1, 5-9, 11, 13, 15, 20-25, 27, 29, 31, 33, 35, 38, 39, 41, 44-49, 51-53, 55 and 56, Applicants argue the following:

a) Lizardi does not teach multiple primers bound to the same ATC, and Lizardi teaches that only a single primer can be bound to an ATC. Applicants admit that Lizardi teaches a secondary primer binding to a secondary ATC in Fig. 12.

b) Even though Lizardi teaches secondary and tertiary primers which bind to TS-DNA, which is amplified from the ATC, and they anneal to the ATC, but Lizardi teaches using these primers only for amplification of TS-DNA, not ATC. Applicants further argue that since the ATC has only a single primer complementary portion, it can bind only a single primer at a time, irrespective of the presence of secondary and tertiary primers.

c) There is no motivation to combine the random primers of Eckstein et al. with Lizardi because Lizardi does not teach multiple P1 primers on the same ATC.

Applicants' analysis relies on only one of the references over which the claims were rejected. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

However, Lizardi does suggest using multiple primers for a single ATC. As admitted by Applicants, the secondary and tertiary primers have binding sites on the ATC, but, for reasons Applicants do not disclose, are forbidden to bind to it, even though they bind to TS-DNA sequences, which are exact replicas of the ATCs. Therefore, if the first, secondary and tertiary primer are present in the reaction mixture with the ATC, one would expect amplification to occur from the secondary and tertiary primers annealed to the ATC simultaneously with the first primer. Therefore, at the very least, Lizardi suggests using multiple primers. The teaching of multiple primers and amplification of circular molecules comes from Landers et al. and the teaching of nuclease resistant nucleotides from Eckstein et al., therefore, the combination of these three references makes claims 1, 5-9, 11, 13, 15, 20-25, 27, 29, 31, 33, 35, 38, 39, 41, 44-49, 51-53, 55 and 56 obvious.

The rejection is maintained.

B) Regarding the rejection of claims 12, 36 and 37 under 35 U.S.C. 103(a) over Lizardi, Landers et al., Eckstein et al. and in view of Rothberg et al., Applicants argue that since claim 1 is patentable over the first three references, the rejection of is improper. Arguments concerning rejection of claim 1 were presented above.

The rejection is maintained.

C) Regarding the rejection of claims 14, 57 and 58 under 35 U.S.C. 103(a) over Lizardi, Landers et al., Eckstein et al. and in view of Navarro et al., Applicants argue that since claim 1 is patentable over the first three references, the rejection of is improper. Arguments concerning rejection of claim 1 were presented above.

The rejection is maintained.

D) Regarding the rejection of claims 12, 36 and 37 under 35 U.S.C. 103(a) over Lizardi, Landers et al., Eckstein et al. and in view of Skerra et al., Applicants argue that since claim 1 is patentable over the first three references, the rejection of is improper. Arguments concerning rejection of claim 1 were presented above.

The rejection is maintained.

Claim Interpretation

4. Applicants defined the term "random primers" on page 13, lines 20-26: "... As used herein, the term "random" means that said oligonucleotide primers (P1) have nucleotide sequences unrelated to the nucleotide sequences of the amplification target circle (ATC) that acts as template for amplification. The result of such a random relationship is that the locations on the ATC at which said random primers hybridize will also be random."

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 5-9, 11, 13, 15, 20-25, 27, 29, 31, 33, 35, 38, 39, 41, 44-49, 51-53, 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lizardi (U.S. Patent No. 5,854,033; cited in the previous office action), Landers et al. (U.S. Patent No. 6,703,228; cited in the previous office action) and Eckstein et al. (Trends in Bioch. Sci., vol. 14(3), pp. 97-100, 1989 ; cited in the previous office action).

A) Regarding claim 1, Lizardi teaches a method of amplification comprising contacting multiple single stranded non-circular random oligonucleotide primers (P1), one or more amplifIcation target circles (ATCs), a DNA polymerase and multiple deoxynucleoside triphosphates (dNTP), under conditions promoting said contacting, wherein an ATC hybridizes to a plurality of said P1 primers, wherein said conditions promote replication of the amplification target circle by extension of the P1 primers to form multiple tandem sequence DNA (TS-DNA) products and wherein at least one such dNTP renders the TS-DNA resistant to nuclease activity following incorporation thereinto (Lizardi teaches amplification of circular DNA molecule by a rolling circle method. The rolling circle amplification (RCA) involves hybridization (= contacting) of a primer (P1) to amplification target circles (ATC) followed by amplification using strand-displacing DNA polymerase, resulting in a DNA molecule with multiple repeats of the ATC, usually referred to as tandem sequences DNA (TS-DNA) (column 19, lines 20-31). In one embodiment of the amplification, strand displacement cascade amplification, (SDCA), secondary and tertiary primers

are used, with sequences complementary to the ATC (col. 25, lines 36-49). The SDCA can be performed simultaneously with RCA, resulting in exponential amplification (col. 28, lines 8-18; col. 26, lines 61-66). Therefore, Lizardi teaches the limitation of multiple P1 primers. Lizardi teaches dNTPs (col. 36, lines 50, 51).

Regarding claims 5-7, Lizardi teaches primers from 10 to 35 nucleotides long (col. 10, line 14), therefore anticipating the limitations of the primers being 2 to 50, 2 to 35 or 2 to 10 nucleotides in length.

Regarding claim 11, Lizardi teaches ATC being a circular, single-stranded DNA molecule, (col. 9, lines 25-29).

Regarding claim 20, Lizardi teaches ATC being a circular, single-stranded DNA molecule, containing between 40 to 1,000 nucleotides (col. 9, lines 25-29), anticipating the limitation of ATC being no larger than 10,000 nucleotides in size.

Regarding claims 22 and 23, Lizardi teaches ATC being a circular, single-stranded DNA molecule, containing between 40 to 1,000 nucleotides (col. 9, lines 25-29), anticipating the limitations of ATC being no larger than about 1,000 nucleotides and no larger than about 100 nucleotides in size.

Regarding claim 24, Lizardi teaches that ATC can be derived from a single-stranded bacteriophage (col. 35, lines 50-59).

Regarding claim 27, Lizardi teaches that radioactive nucleotides can be used in the amplification (col. 21, lines 22-25).

Regarding claim 31, Lizardi teaches that primers may include modified nucleotides to make them exonuclease-resistant (col. 10, lines 24-28; col. 13, lines 27-31). Therefore Lizardi teaches exonuclease activity.

Regarding claim 33, Lizardi teaches adding exonuclease to digest unligated circles (col. 10, lines 28-33; col. 24, lines 41-61).

Regarding claim 35, Lizardi teaches that modified nucleotides can be used in the amplification (col. 21, lines 22-25).

Regarding claims 38 and 39, Lizardi teaches primers which include modified nucleotides to make them exonuclease-resistant (col. 10, lines 24-28; col. 13, lines 27-31).

Regarding claims 44, 45 and 47, Lizardi teaches that phophorothioate nucleotides are positioned at the 5'-end of the primer to make it exonuclease-resistant (col. 10, lines 24-28; col. 13, lines 27-31). Therefore Lizardi anticipates the limitations of an exonuclease-resistant primer containing at least one nucleotide which makes it resistant to exonuclease activity, a modified nucleotide and a phosphorothioate nucleotide.

Regarding claim 48, Lizardi teaches three or four phosphorothioate nucleotides (col. 10, lines 24-28; col. 13, lines 27-31).

Regarding claim 49, Lizardi teaches the phosphorothioate nucleotides being at the 5' end of the primer (col. 10, lines 24-28; col. 13, lines 27-31).

Regarding claims 51 and 52, Lizardi teaches the following DNA polymerases to be used: bacteriophage ϕ 29 DNA polymerase, phage M2 DNA polymerase, VENT DNA polymerase, Klenow fragment of DNA polymerase I, T5 DNA polymerase, PRD1 DNA polymerase, T4 DNA polymerase holoenzyme (col. 17, lines 66-67, col. 18, lines 1-11). Therefore, since the claim language links 3',5'-exonuclease activity with these enzymes, and Lizardi specifically teaches them, Lizardi inherently teaches polymerases with 3' -> 5' exonuclase activity.

Regarding claim 53, Lizardi teaches bacteriophage ϕ 29 DNA polymerase (col. 17, lines 66-67, col. 18, lines 1-11) and exonuclease-resistant primers (col. 10, lines 24-28; col. 13, lines 27-31).

Regarding claims 36 and 37, Lizardi teaches oligonucleotides attached to solid support, including glass (col. 14, lines 34-43, 65-67; col. 15, lines 1-10).

B) Lizardi does not teach random primers, nucleotides which confer nuclease resistance to an amplification product, duplex DNA, denaturation of duplex DNA, DNA larger than 10,000 nucleotides, DNA with unknown sequence, dNTPs being phosphorothioate nucleotides, modified nucleotide being a 3'-terminal nucleotide or a DNA polymerase which does not exhibit 3' -> 5' exonuclease activity.

C) Regarding claim 1, Landers et al. teach generation of reduced complexity genomes by amplification of genomic double-stranded DNA circles (YACs) with multiple arbitrary (= random) primers (col. 17, lines 28-42 and 60-64).

Regarding claims 8 and 9, Landers et al. teach that the sequence of the random primers contains the N_x residues of the DOP-PCR primers (col. 17, lines 35-39). Landers et al. teach DOP-PCR primers containing x N residues, where x is an integer from 0 to 9, therefore Landers et al. teach hexamers and octamers.

Regarding claim 13, Landers et al. teach YACs (Yeast Artificial Chromosomes), which are double-stranded circles (col. 17, lines 64, 65).

Regarding claim 15, Landers et al. teach denaturation of double-stranded DNA during PCR amplification (col. 14, lines 14-36; col. 62, lines 36-43; col. 63, lines 16-25).

Regarding claim 21, Landers et al. teach YACs (Yeast Artificial Chromosomes) carrying inserts of 300,000-400,000 base pairs (col. 17, lines 64-66), therefore Landers et al. teach ATCs larger than 10,000 nucleotides in size.

Regarding claim 25, Landers et al. teach amplification of unknown sequences (col. 17, lines 31-34).

Regarding claims 55 and 56, Landers et al. teach amplification using Taq DNA polymerase (col. 14, lines 51-54). Therefore, since the claim language connects 3',5'-exonuclease activity with Taq DNA polymerase, and Landers et al. teach Taq DNA polymerase, they inherently teach a DNA polymerase without 3'5'-exonuclease activity.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have included random primers and DNA molecules of Landers et al. in the method of Lizardi. The motivation to do so, provided by Landers et al., would have been that random primers allowed for amplification of unknown DNA sequences (col. 17, lines 31-34), and using double-stranded DNA allowed for reducing complexity of genomic samples for purposes of genotyping related to screening of populations for diseases (col. 10, lines 13-24).

D) Landers et al. do not teach nucleotides which confer nuclease resistance to an amplification product, dNTPs being phosphorothioate nucleotides, modified nucleotide being a 3'-terminal nucleotide.

E) Regarding claims 1 and 29, Eckstein et al. teach that deoxynucleoside 5'-O-(1-thiotriphosphates), or phoshorothioates, are substrates for DNA and RNA polymerases (Abstract; page 97, first paragraph).

Regarding claim 41, Eckstein et al. teach exonuclease III with 3',5'-exonuclease activity (page 97, fourth paragraph).

Regarding claims 46 and 47, Eckstein et al. teach that incorporation of single phosphorothioate group at the 3' end of a DNA strand prevents its degradation by exonuclease III, an enzyme with 3',5' activity (page 97, fourth paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used phosphorothioate dNTPs of Eckstein et al. in the amplification method of

Lizardi and Landers et al. The motivation to do so, provided by Eckstein et al., would have been that phosphorothioate containing DNA was resistant to degradation by nucleases and the sulfur atom conferred many favorable chemical properties (Abstract).

7. Claims 12, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lizardi (U.S. Patent No. 5,854,033; cited in the previous office action), Landers et al. (U.S. Patent No. 6,703,228; cited in the previous office action) and Eckstein et al. (Trends in Bioch. Sci., vol. 14(3), pp. 97-100, 1989; cited in the previous office action) as applied to claim 1 above, and further in view of Rothberg et al. (U.S. Patent No. 6,274,320; cited in the previous office action).

A) Claim 12 is drawn to a duplex DNA circle having at least one nick, claim 36 is drawn to at least one P1 primer attached to a solid support and claim 37 is drawn to the solid support being glass or plastic.

B) Lizardi teaches oligonucleotides attached to solid support, the support being glass or plastic. Lizardi, Landers et al. and Eckstein et al. do not teach duplex DNA circles with at least one nick or primers attached to solid support.

C) Regarding claim 12, Rothberg et al. teach templates are open or closed circles (col. 3, lines 57-60), and nicked double-stranded circles (col. 12, lines 26-35).

Regarding claim 36, Rothberg et al. teach amplification of circular templates by rolling circle amplification using primers attached to a solid support (Fig. 1; col. 3, lines 66,67; col. 4, lines 1-10 and 29-37; col. 5, lines 6-20; col. 11, lines 54-67; col. 12, lines 1-9).

Regarding claim 37, Rothberg et al. teach solid supports being a DNA chip or a glass slide (col. 19, lines 40-43) or an optical fiber (col. 20, lines 15-18).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used primers attached to a solid support of Rothberg et al. in the method of

Lizardi, Landers et al. and Eckstein et al. The motivation to do so, provided by Rothberg et al., would have been that amplification of circular templates on solid support allowed for determination of nucleic acid sequence without the need for cloning the templates and determination of rare nucleic acids with high sensitivity (col. 5, lines 22-28).

8. Claims 14, 57 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lizardi (U.S. Patent No. 5,854,033; cited in the previous office action), Landers et al. (U.S. Patent No. 6,703,228; cited in the previous office action) and Eckstein et al. (Trends in Bioch. Sci., vol. 14(3), pp. 97-100, 1989; cited in the previous office action) as applied to claim 1 above, and further in view of Navarro et al. (J. Virol. Meth., vol. 56, pp. 59-66, 1996; cited in the previous office action).

A) Claim 14 is drawn to ATC being single stranded RNA circle, claim 57 is drawn to DNA polymerase being a reverse transcriptase and claim 58 is drawn to the ATC being RNA and DNA polymerase being a reverse transcriptase.

B) Lizardi, Landers et al. and Eckstein et al. do not teach RNA circles or a reverse transcriptase.

C) Navarro et al. teach amplification of circular RNA viroids using random hexamers and AMV reverse transcriptase (Fig. 1; page 59, first paragraph; page 60, paragraphs 4 and 5; page 61, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the amplification of RNA circles of Navarro et al. in the method of Lizardi, Landers et al. and Eckstein et al. The motivation to do so, provided by Navarro et al., would have been that amplification of circular pathogenic RNA provided means of cloning the RNAs from small amounts of sample with unknown sequence (page 60, second paragraph).

9. Claims 32, 42 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lizardi (U.S. Patent No. 5,854,033; cited in the previous office action), Landers et al. (U.S. Patent No. 6,703,228; cited in the previous office action) and Eckstein et al. (Trends in Bioch. Sci., vol. 14(3), pp. 97-100, 1989; cited in the previous office action) as applied to claims 1, 31 and 38 above, and further in view of Skerra (Nucleic Acids Research, Vol. 20, pp. 3551-3554, 1992; cited in the previous office action).

A) Claims 32 and 42 are drawn to a polymerase with 3'-> 5' exonuclease activity and claim 59 to the use of a mixture of primers sensitive to and resistant to exonuclease activity.

B) Lizardi, Landers et al. and Eckstein et al. do not teach primers resistant to 3'-> 5' exonuclease activity, the resistance being conferred by a phosphorothioate nucleotide at the 3'-end of the primer or the use of a mixture of exonuclease-sensitive and exonuclease-resistant primers in the amplification reaction.

C) Skerra teaches that incorporation of a phosphorothioate nucleotide at the 3'-end of the primer renders it inactive to the 3'-> 5' exonuclease activity of DNA polymerases such as Vent and Pfu. The reference also teaches use of a mixture of exonuclease-sensitive and exonuclease-resistant primers in the amplification reaction (Abstract; page 3553; Fig. 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used primers of Skerra with phosphorothioate nucleotides at the 3'-end in the amplification method of Lizardi, Landers et al. and Eckstein et al. The motivation to do so, provided by Skerra, would have been that the 3'-end phosphorothioate nucleotide rendered the primers resistant to 3'-> 5' exonuclease activity of the polymerase used in the reaction, resulting in an improved yield of the amplification product (page 3553, third paragraph).

10. No claims are allowed.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TS
February 8, 2005

JEFFREY FREDMAN
PRIMARY EXAMINER
2/1/05